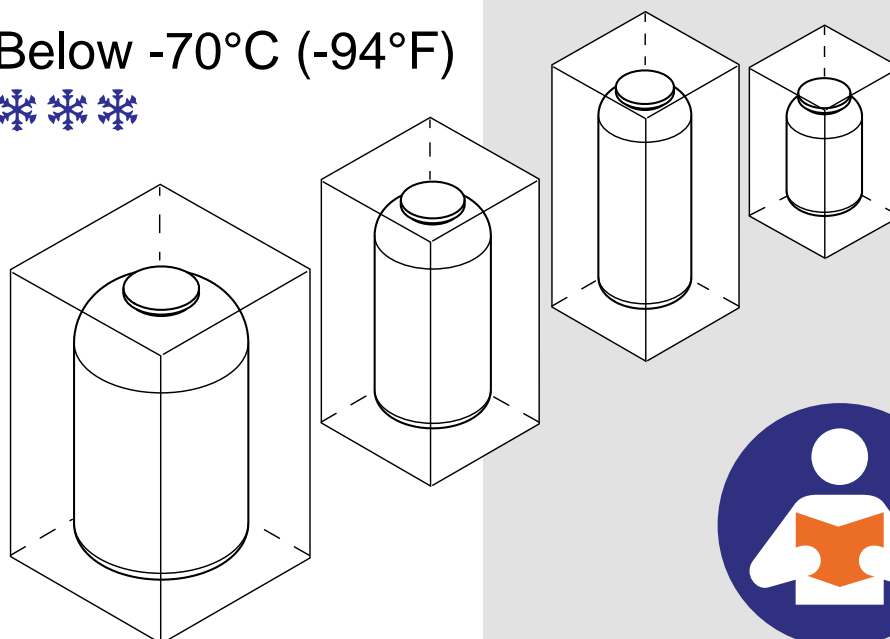


Envirotainer[®]

The Active Cold Chain

Below -70°C (-94°F)



User Manual

CryoSure[®] systems

X1, X2, X5, X11

Doc No. UM-CRYO-3030

Version 1

www.envirotainer.com

RECORD OF REVISION

VER. NO.	REVISION
1	<p>REVISED:</p> <ul style="list-style-type: none"> • 2.3 Cleanliness of product: New chapter. • Table 1 Measurements and weight: New rows with additional product data. • General editorial improvements: <ul style="list-style-type: none"> • Terminology of CryoSure^o systems has been set and updated from unit, technology etc. • Clarified intended use of product, to include cell & gene therapy and biospecimens. • Clarified/changed wording in Table 1. <ul style="list-style-type: none"> • Autonomous duration with an * reference to bottom of the table. • Changed wording in Table 1. "Target" to "Average". • Corrected measurements in "outer dimensions of box". • Corrected external dimension of X11. • Clarified "Total weight" to "Total weight (excl. product load)". • Removed specified carriers. • Changed wording of pouch and envelop to folder. • Clarified definition of deep frozen to be below -70°C (-94°F). • Clarified that customer normally never are to handle dry ice when using the CryoSure^o system. • Changed header in chapter 3.3 from "Remaining dry ice time" to "Dry ice duration". • Changed header in chapter 3.4 from "Remaining dry ice time look-up" to "Calculating remaining dry ice time". • Changed publisher on backside cover from Envirotainer Engineering AB to Envirotainer AB. • Updated illustrations. <ul style="list-style-type: none"> • Removed branding on cardboard box. • Moved shipping label to be positioned on same side as other labels. • Removed superfluous figures.

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1. INTRODUCTION

The CryoSure° system is designed for global shipping and storage of pharmaceutical products, clinical trial materials, vaccines, cell & gene therapy, biospecimens and specialty medicines that are required to be kept below -70°C (-94°F).

The CryoSure° system uses a unique patented technology combined with dry ice. It is a **reusable** shipping system which offers both mechanical protection of the shipped product and maintains load space temperature below -70°C (-94°F) (average between -74°C and -80°C / -101°F and -112°F).

- Maintains temperature control consistently below -70°C (-94°F)
- Suitable for any destination, domestic or international, and by ground or air, covering the entire shipment duration including delays and customs without the need to re-charge
- Provides mechanical protection during transport by ground or air

The CryoSure° system comes in four different sizes, with product space volume from 1L to 10.8L. The temperature control duration is intended to last throughout the shipment without recharging.

These systems will be pre-charged with dry ice at an Envirotainer facility and be delivered to a second location where temperature-sensitive materials can be loaded into the vessel for transit or storage.

1.1 OVERVIEW

The CryoSure° product line consist of four different sizes.

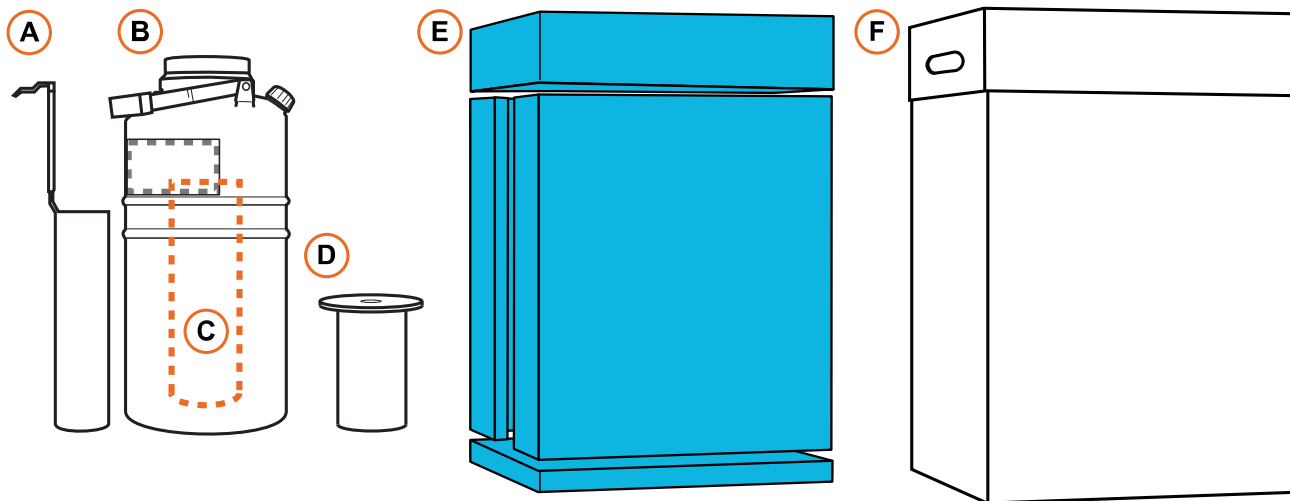
Table 1 Measurements and weight

CryoSure° system	X1	X2	X5	X11
Autonomous duration*	>7 days	>20 days	>10 days	>10 days
Average sublimation rate	0,005 kg / hour	0,006 kg / hour	0,009 kg / hour	0,019 kg / hour
Payload opening	Ø 9 cm (Ø 3.54")	Ø 9 cm (Ø 3.54")	Ø 15.2 cm (Ø 5.98")	Ø 21,6 cm (Ø 8.50")
Dry-ice payload	1 kg (2.20 lb.)	3,7 kg (8.16 lb.)	3,5 kg (7.71 lb.)	7 kg (15.43 lb.)
Product payload	1 L (20 vials)	1.6 L (75 vials)	4.9 L (200 vials)	10.8 L (500+ vials)
Outer dimensions of box (WxLxH)	23 x 23 x 37,2 cm (9.05" x 9.05" x 14.64")	34 x 34 x 58,1 cm (13.38" x 13.38" x 22.87")	34 x 34 x 58,1 cm (13.38" x 13.38" x 22.87")	42 x 42 x 63 cm (16.53" x 16.53" x 24.80")
Total weight (excl. product load)	5,03 kg (11.09 lb.)	8,67 kg (19.11 lb.)	12,12 kg (26.72 lb.)	19 kg (41.89 lb.)

* When exposed to ISTA 7D summer profile

1.2 TECHNICAL DETAILS

A complete CryoSure^o system is comprised of the following components:



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Fig. 1 The CryoSure^o system.

Table 2 CryoSure^o system features

Pos	Name	Description
A	Product holder (standard for X2 or X5)	Cylindrical stainless-steel container with handle for loading materials into, removing materials from, or holding materials within the storage zone of the CryoSure ^o vessel
B	CryoSure ^o vessel	Insulated aluminum container that holds the dry ice refrigerant and material to be preserved
C	Product space	To place product holder in
D	Insulating lid	Cap and insulating cork used to close the CryoSure ^o vessel opening while allowing carbon dioxide vapor from sublimating dry ice inside the CryoSure ^o vessel to still vent freely outside the vessel
E	Foam inserts	Reusable packaging positioned between the CryoSure ^o vessel and cardboard box that protects the vessel from handling damage: (one (1) bottom, one (1) top, and two (2) side pieces)
F	Cardboard box	External packaging Shipping, safety, and regulatory labels are applied to the exterior of the cardboard box as appropriate

1.3 INTENDED USE

Pre-charged CryoSure° systems are delivered with dry ice already loaded inside. In normal operation, users are never required to handle dry ice.

The CryoSure° system is designed for global shipping and storage of pharmaceutical products, clinical trial materials, vaccines, cell & gene therapy, biospecimens and specialty medicines that are required to be kept below -70°C (-94°F).

The CryoSure° system offers both mechanical protection of the shipped product and maintains load space temperature below -70°C (-94°F) throughout the shipping duration.

Refer to **2. Safety**.

! IMPORTANT!

Biological materials used with the CryoSure° systems are limited to Biological Substance Category B materials specified under UN 3373 and exceptions defined in IATA 3.6.2.2.3.

No pathogenic Category A materials (UN 2814, UN 2900) or medical or clinical wastes (UN 3291) shall be used with the CryoSure° systems.

1.4 OPERATING CONDITIONS

Ambient temperatures, humidity, improper orientation of system and mechanical shock does not impact the CryoSure° system temperature levels.

It is suitable for any location or environment with temperature below 35°C (95°F), independent of orientation of box.

2. SAFETY

- Read the manual before handling and operating the CryoSure[°] system.
- Read the Safety Data Sheet for dry ice (**UN1845**).
- Pay attention to warning stickers and texts attached to the CryoSure[°] system.

2.1 SHIPPING REGULATIONS

The United States Department of Transportation (**DOT**) and related international government agencies regulate shipments containing dry ice and biological materials. In addition, the International Air Transport Association (**IATA**) maintains standards that guide airline polices regarding dry ice and biological material shipments. Users of a pre-charged CryoSure[°] system should review and follow all appropriate government and carrier requirements for labeling and packaging shipments containing dry ice or biological materials.

2.2 SYMBOLS ON THE CRYOSURE[°] SYSTEM

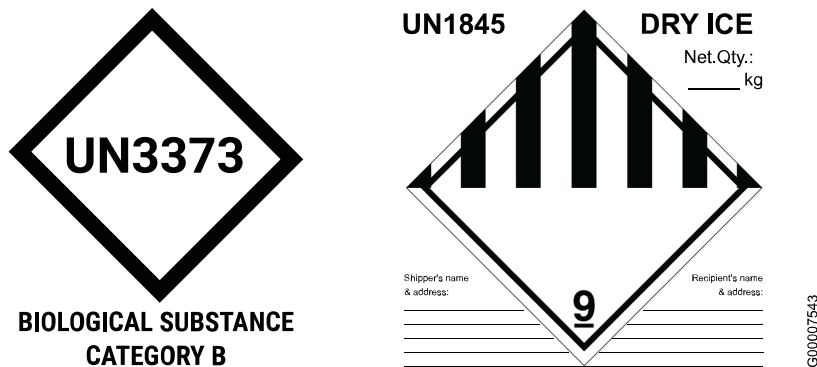


Fig. 2

! IMPORTANT!

All **UN3373** biological materials, whether shipped by ground or air transport, must be packed within the CryoSure[°] system as described in IATA Packing Instruction 650 or ADR Packing Instruction P650 in a leak-proof primary receptacle and a leak-proof secondary receptacle containing the primary receptacle(s) and an absorbent in sufficient quantity to absorb the entire contents of any liquid materials in the primary receptacle (s) with the primary receptacle and secondary receptacles maintaining their integrity at the temperature of dry ice and the temperatures which could result if refrigeration were lost.

UN1845 (Dry ice) is solidified carbon dioxide. At atmospheric pressure, dry ice sublimates to carbon dioxide vapor at approximately -78.5°C (-109.3°F). Dry ice is very cold, and contact with dry ice or areas cooled by dry ice can cause frostbite. The CryoSure[°] pre-charged system is delivered with dry ice already loaded inside. In normal operation, it should not be necessary for users of a pre-charged CryoSure[°] system to handle dry ice. The interior spaces and surfaces of a pre-charged CryoSure[°] are very cold, and users are advised to wear appropriate gloves when interacting with the interior of the dry ice vessel or items recently removed from the interior. The carbon dioxide evolved by sublimation of dry ice can create potentially hazardous carbon dioxide-enriched and/or oxygen-deficient atmospheres. Users of dry ice or dry ice-containing systems are recommended to evaluate the potential for atmospheric hazards in their working environment and take appropriate steps to address such hazards (for example, by using air monitoring devices and adequate ventilation).

2.3 CLEANLINESS OF PRODUCT

The CryoSure^o system is cleaned using VIRKON™ solution and Isopropyl alcohol according to Envirotainer instruction **SOP-ENV-0229** and **SOP-ENV-0234**.

3. USING THE CRYOSURE[°] SYSTEM

3.1 PREPARING A SHIPMENT

It is recommended to have the product pre-conditioned to -70°C (-94°F) or below -78.5°C (-109.3°F) for the CryoSure[°] system to operate within the specified temperature regulating duration. Using the CryoSure[°] to cool the product will reduce the temperature regulating duration.

3.2 OPERATING INSTRUCTIONS

1. Product loading, **3.2.1 Product loading.**
2. Shipping CryoSure[°], **3.2.2 Shipping of loaded product.**
 - Remove old labels and documents.
 - Prepare new labels and documents for cardboard box.
3. Receiving CryoSure[°] and removing products, **3.2.3 Product unloading.**
4. Returning/shipping CryoSure[°] to Envirotainer/new destination, **3.2.4 Returning of empty product.**
 - Remove any biological product materials and associated packaging from the CryoSure[°] vessel.
 - Remove old labels and documents.
 - Prepare new labels and documents for cardboard box.

3.2.1 PRODUCT LOADING

1. Inspect the outer packaging. If the cardboard box is too worn for use, contact Envirotainer for support.

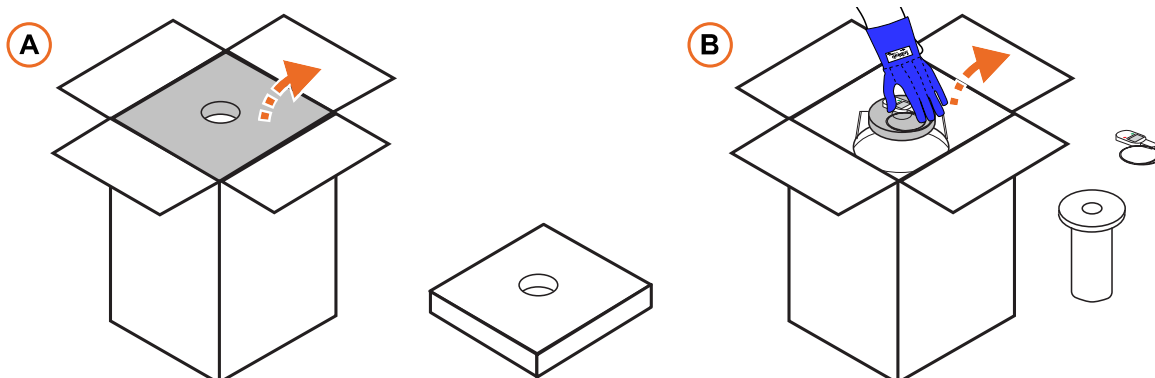


Fig. 3

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2. Opening the box:

2a. Open the box and set aside the top foam.

! IMPORTANT!
DO NOT DISCARD THE FOAM

2b. Wearing safety gloves, remove the CryoSure° vessel lid. Place the lid to one side, together with the data logger and probe (if any).

! DANGER!
DO NOT DISCARD THE LID

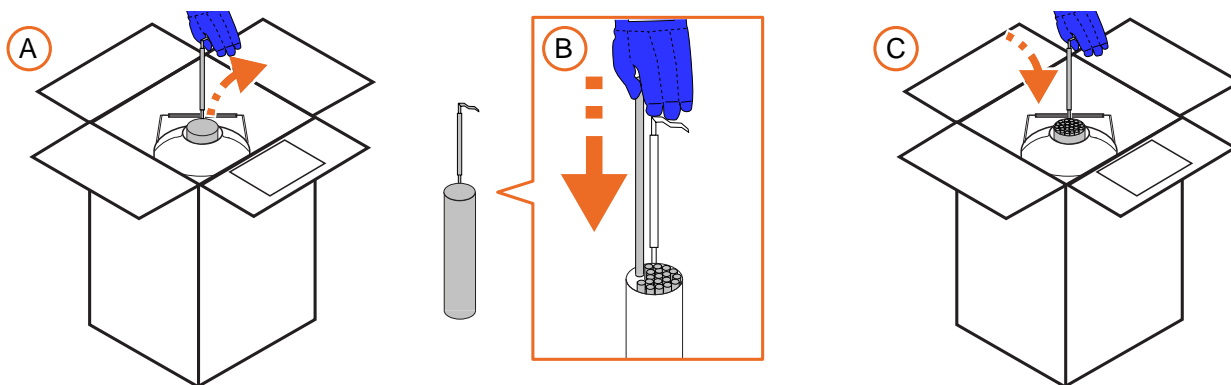


Fig. 4

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3. Loading the product:

3a. Lift the product holder by its handle and remove it from the CryoSure° vessel.

3b. Load the product into the product holder. Follow all applicable government and carrier requirements for packaging the product.

3c. Lift the product holder into the CryoSure° vessel.



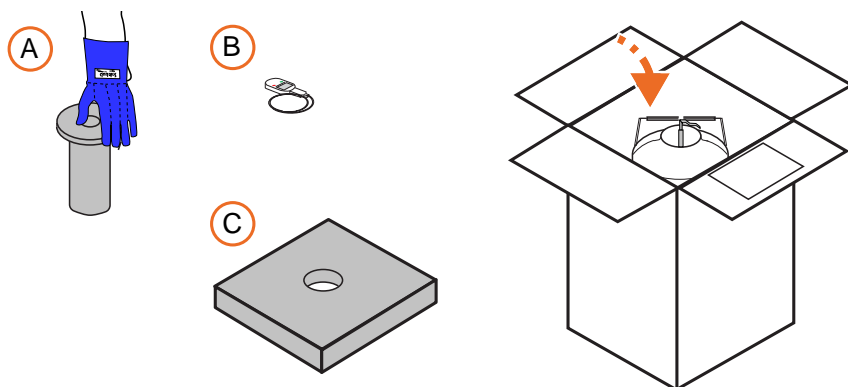


Fig. 5

4. Place the following items back in place:

- 4a.** lid (wearing safety gloves)
- 4b.** data logger and probe (if any)
- 4c.** top foam.

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3.2.2 SHIPPING OF LOADED PRODUCT

! IMPORTANT!

After the CryoSure° vessel has been loaded with product and properly packaged with all required components, labels need to be applied to the exterior of the cardboard box in accordance with government (e.g., US DOT, EU ADR) regulations and carrier (e.g., IATA) requirements.

Please ensure that all needed documents according to the correspondent regulations are on hand (for example shippers declaration, pro forma invoices and packing lists)

1. Remove or cover all labels on the cardboard box:
 - the label of the parcel carrier
 - the dangerous goods label (**UN1845**) where you are notified as **consignee**

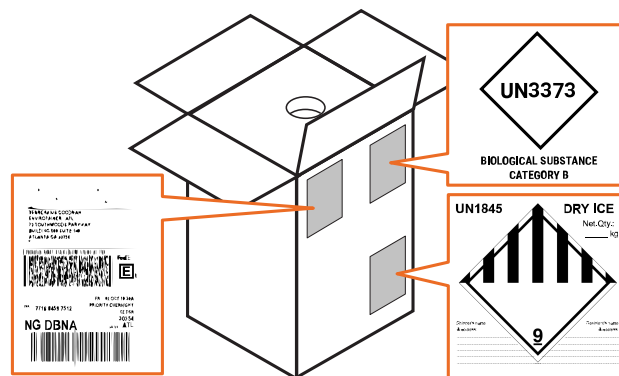


Fig. 6

2. Apply the labels to the exterior of the box in accordance with government regulations and carrier requirements.
3. Ensure that the following documents are in the folder:
 - original shipper’s declaration (according to US DOT, EU ADR or IATA regulations)
 - original pro-forma invoice
 - original packing list
4. Close and seal the cardboard box with a clear tape.
5. Take necessary steps in order to inform selected carrier that the parcel is ready for pick-up.

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3.2.3 PRODUCT UNLOADING

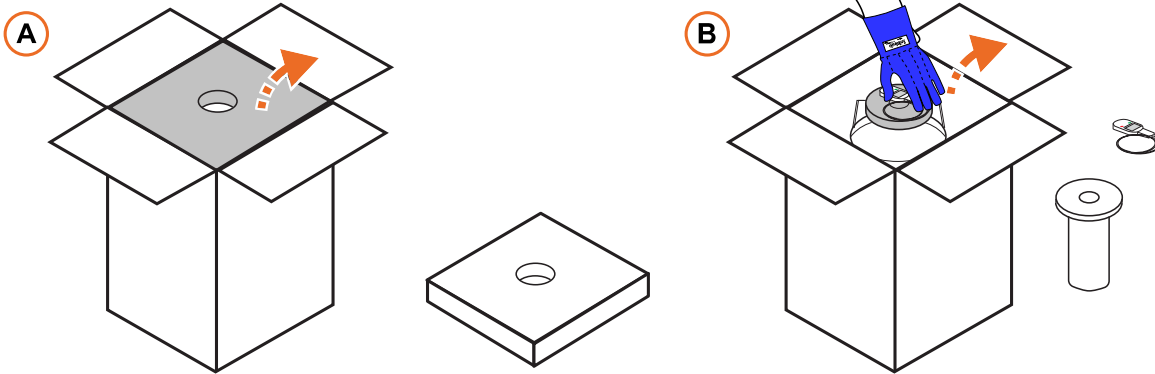


Fig. 7

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1. Unpacking:

1a. Open the box and set aside the top foam.

! IMPORTANT!
DO NOT DISCARD THE FOAM

1b. Wearing safety gloves, remove the CryoS sure^o vessel lid. Place the lid to one side.

! CAUTION!
DO NOT DISCARD THE LID

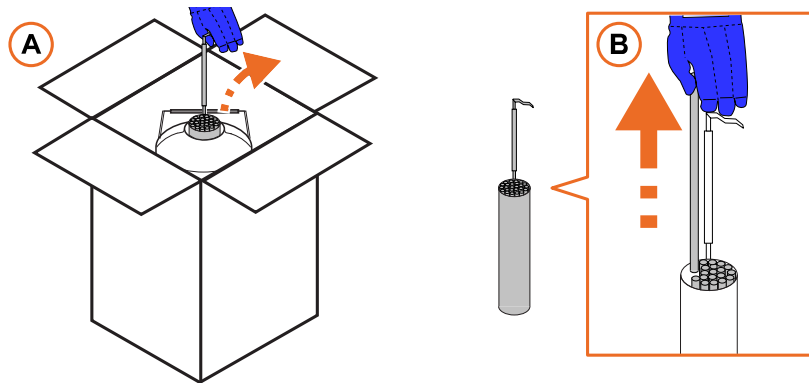


Fig. 8

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2. Unloading product:

2a. Lift the product holder by its handle and remove it from the CryoS sure^o vessel.

2b. Remove the product from the product holder. Store or use the product as defined by procedures.

3. Prepare the next shipment.

- If loading new product into the CryoS sure^o vessel, follow step **3b** and onwards of the **3.2.1 Product loading** procedure to prepare the shipment.
- If sending the CryoS sure^o vessel to its next destination, follow step **3c** and onwards of the **3.2.1 Product loading** procedure to prepare the shipment.

3.2.4 RETURNING OF EMPTY PRODUCT

If you have booked a collection service from Envirotainer, a prepaid shipping return label is included in a folder on the inside of the cardboard box. If you have not pre-booked the collection service, contact Envirotainer support to place an order for the service. Otherwise, follow steps 1 and 2 below to prepare the CryoSure° system for return.

1. Remove any biological product materials and associated packaging from the CryoSure° vessel.
2. Remove or cover all labels on the cardboard box:
 - the label of the parcel carrier
 - the dangerous goods label (**UN1845**) where you are notified as **consignee**
 - the dangerous goods label (**UN 3373**)

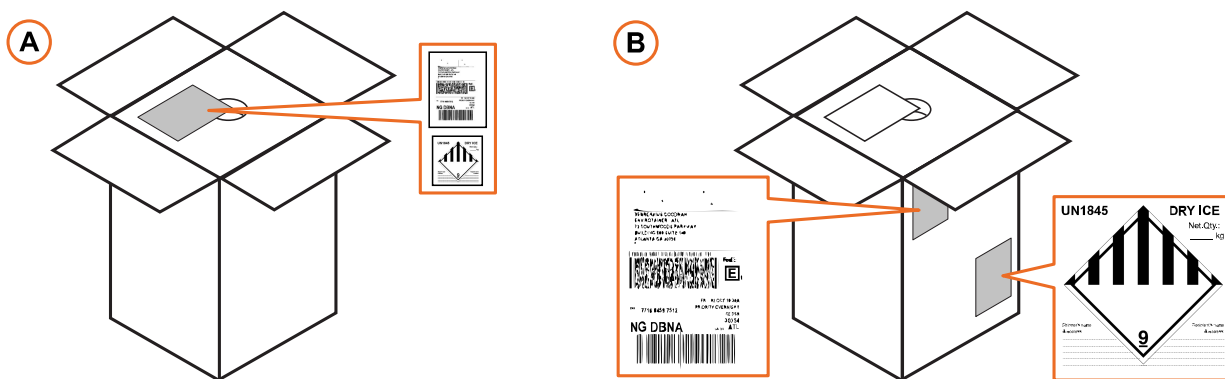


Fig. 9

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3. Preparing the documents and labels.
 - 3a. Remove the folder “Return” from the cardboard box. In the folder you find the pre-printed labels you need for returning the CryoSure° product:
 - the pre-paid label of the parcel carrier, where you are notified as **Sender**
 - the dangerous goods label (**UN1845**), where you are notified as **Shipper**
 - 3b. Peel the and apply both labels and put them on the cardboard box.

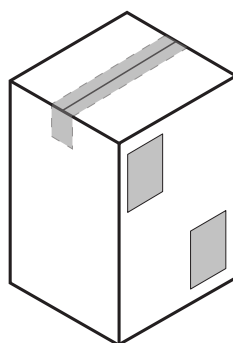


Fig. 10

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4. Close the cardboard box, and seal with a clear tape.
5. Inform Envirotainer that the CryoSure° system is ready for pick-up. Upon your advice, Envirotainer arranges with the parcel carrier a pick-up.

3.3 REMAINING DRY ICE TIME

The remaining dry ice duration for a pre-charged CryoSure^o system can be estimated at any time by weighing the system on a scale following the procedures in **3.3.1 Calculating remaining dry ice time**.

Please note the following:

- The result of these procedure is only an estimate and subject to potential errors should the weight measurement be performed incorrectly or the CryoSure^o system be damaged or used improperly.
- Before performing the measurement ensure that the scale can accurately measure to the nearest 0,045 kg (0.1 lb.) or over a range from 0 to 23 kg (0 to 50 lb.).

3.3.1 CALCULATING REMAINING DRY ICE TIME

1. Zero the scale with nothing on it so that the empty scale reading is 0.
2. Weigh the complete CryoSure^o system on the scale.
 Ensure that all package components are included during the weighing process: product holder, CryoSure^o vessel, insulating lid, temperature data logger and probe (if any), foam inserts and cardboard box.
 It is OK to keep product in the product holder inside the CryoSure^o vessel during the weighing process.
3. Use the following table to estimate the minimum dry ice time remaining:

Table 3 Remaining dry ice time estimation

CryoSure^o											
X1			X2			X5			X11		
Weight		Remaining time	Weight		Remaining time	Weight		Remaining time	Weight		Remaining time
kg	lb.	days	kg	lb.	days	kg	lb.	days	kg	lb.	days
N/A			11.1	24.5	21.5	13.6	30.0	10.5	N/A		
			10.2	22.5	15.5	12.7	28.0	7.0			
			9.3	20.5	10.0	12.0	26.5	4.5			
			8.6	19.0	5.5	11.4	25.0	2.5			
			8.2	18.0	2.5	11.1	24.5	1.5			
			8.0	17.5	1.0	10.9	24.0	0.5			

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